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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/770,562	01/26/2001	William J. Curatolo	8191-87018-01	8513

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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1613	

NOTIFICATION DATE	DELIVERY MODE
08/26/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	09/770,562	CURATOLO ET AL.	
	Examiner	Art Unit	
	BLESSING FUBARA	1613	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1,4,23,28-38,49-51 and 53-58* is/are pending in the application.

5a) Of the above claim(s) *28-35,38 and 57* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1,4,23,36,37,49-51,53-56 and 58* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The examiner acknowledges receipt of request for continued examiner under 37 CFR 1.114 after the BPAI decision of 03/29/2011, power of attorney, amendment and remarks, all filed 5/18/2011. Claims 1, 36, 37, 49-51 and 53-56 are amended, New claims 57 and 58 are added. Claims 28-35 and 38 remain withdrawn from consideration. Claims 1, 4, 23, 28-38, 49-51 and 53-58 are pending.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114 was filed in this application after a decision by the Board of Patent Appeals and Interferences, but before the filing of a Notice of Appeal to the Court of Appeals for the Federal Circuit or the commencement of a civil action. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 05/18/2011 has been entered.

3. The amendment: Claims 1, 4, 23, 36, 37, 49-51 and 53-56 have been amended to recite spray dried solid dispersion instead of the composition of matter comprising spray dried solid dispersion as was recited in claim 1 that was appealed on 12/18/2009.

4. However, a spray dried solid dispersion refers to a product or composition that is derived from spray drying a composition. For example, properly using the instant specification as a dictionary for a spray dried solid dispersion, it is clear that spray dried solid dispersion is obtained by "forming a solution comprising (i) HPMCAS, (ii) a sparingly water-soluble drug,

and (iii) a solvent in which both (i) and (ii) are soluble; and spray drying said solution." By the same token a prior art that forms a solution of HPMCAS and sparingly water-soluble drug in a solvent in which both the polymer and the drug are soluble and then removing the solvent by spray drying the solution would inherently produce a spray dried dispersion. Thus, in spite of the amendment, the prior art used to finally reject the claims on 11/09/2009 are still applicable to the claims amended in the RCE of 5/18/2011.

5. New Claim 57: On 01/31/2008, applicant elected ziprasidone for prosecution of the claims; following that election, claims 28, directed to phosphorylase inhibitor, claim 31 directed to lipoxygenase inhibitor, claim 33, directed to corticotropic releasing hormone (CRH) inhibitor, and claim 38, directed to griseofulvin, nifedipine and phenytoin were withdrawn from consideration. Applicant has now resubmitted these claims combined in one claim as new claim 57, claim limitations that were not examined and not finally rejected but withdrawn. Therefore, claim 57 joins claims 28-35 and 38 as being withdrawn from consideration, withdrawal being without traverse because election was made without traverse on 01/31/2008 in view of the fact applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). See also page 2 of 19 of the Brief filed 12/18/2009.

6. New Claim 58: The recitation that the drug in the spray dried solid dispersion is supersaturated in an inherent outcome of spray drying for the production of spray dried solid dispersion. There is nothing in applicant's specification that leads the artisan to a different understanding of the supersaturated nature of the drug in the solid dispersion. Therefore, the prior art used to finally reject the claims on 11/09/2009 are still applicable.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 1, 4, 23, 49-51 and 53-56 and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by Miyajima et al. (EP 0 344 603). 1, 4, 23, 28-38, 49-51 and 53-58

9. Miyajima describes a composition comprising NZ-105 and HPMCAS (page 3, lines 16 and 17). Miyajima describes preparing the composition by dissolving NZ-105 and HPMCAS in an organic solvent and removing the solvent by vacuum drying, spray drying or freeze drying to yield compositions that have remarkably enhanced bioavailability (page 3, lines 16-20; page 4, lines 56-58) with solid dispersions resulting from spray-drying. NZ-105, is a dihydropyridine phosphonic acid derivative drug that is poorly soluble in water (abstract; page 2, lines 14-35; page 3, lines 6-9). 1-7 parts or 3-5 parts by weight of HPMCAS are used per 1 part by weight of NZ-105 (page 5, lines 8 and 9) so that the ratio of the drug to polymer in Miyajima is 1:1 to 1:7 or 1:3 to 1:5 are species of the broader ratio of 1:0.4 to 1:20 and the narrower range or species anticipates the broader range meeting the drug polymer ratio of claims 1, 55 and 56. Claim 51 is a product by process claim and the claim is thus met by the composition of Miyajima. For claim 1, parts (a) and (b) are the properties of the dosage form. Claim 1 recites spray dried dispersion which in claim 4 is amorphous when undispersed and the recitation in claim 4 is also directed to

the properties of the dosage form. The solid dispersion of Miyajima is also spray dried so that the limitation of spray dried solid dispersion is met. Claims 4, 49, 53 and 54 recite the properties of the composition so that the composition of Miyajima meets the claims. The solvent is removed by vacuum drying, spray-drying or freeze-drying and the dried product is inherently free of solvent and Miyajima did not say that the product has associated solvent so that claim 50 is met and further because the spray dried solid dispersion of both the claims and that of the prior art are prepared by the same process. The particle size of 100-400 or 150-300 mesh of the Miyajima particles encompasses the particles size of 100 micron since 400 and 300 mesh sizes are less than 100 micron so that claim 23 is met. For new claim 58, because the spray dried solid dispersion of the claims and the prior art are prepared by the same process, the spray dried solid dispersion of Miyajima is inherently supersaturated in the drug.

10. The spray dried solid dispersion containing the drug and the HPMCAS meets the limitation of the amended claims where the spray dried solid dispersion consists of the drug and polymer and specifically, Miyajima dissolves the drug and HPMCAS in common solvent and removes the solvent by spray drying.

11. Claims 1, 4, 49-51 and 53-56 are rejected under 35 U.S.C. 102(a) as being anticipated by Kigoshi et al. (EP 0 784 974).

12. Kigoshi describes solid dispersions containing xanthine derivatives and polymer (title; abstract; page 2, lines 21, 22, 44, 45); the xanthine derivatives are slightly soluble in water (page 2, lines 21 and 22) meeting the sparingly water soluble drug of the claims; the polymer can be a cellulose derivative (page 3, line 58) with enteric coating polymers preferred (page 4, line 5) and hydroxypropylmethyl cellulose acetate succinate (HPMCAS) is one the preferred derivatives

named (page 4, line 8) meeting the requirements of claim 1. One of the processes of removing the solvent from the formation of the solid dispersion is by spray-dry granulator (page 4, line 38) and the resulting granules/particles are isolated (page 4, lines 49, 50). The ratio of the xanthine derivatives of compound I to the polymer ranges from 3:1 to 1:5 (page 4, lines 12, 13) with the ratio of 1:5 intersecting points within the recited ratio of from 1:0.4 to 1:20 of the claims; also a ratio of 1:1 is preferred (page 4, line 15); so that disclosed ratio, a species of the claimed ratio, meets the requirements of claims 1, 55 and 56. Claim 1 recites spray dried dispersion which in claim 4 is amorphous when undispersed and the recitation in claim 4 is also directed to the properties of the dosage form. Claims 4, 49, 53 and 54 recite the properties of the composition so that the composition of Kigoshi meets the claims. Claim 51 is a product by process claim and the claim is thus met by the composition of Kigoshi. Claim 1 recites spray dried dispersion which in claim 4 is amorphous when undispersed and the recitation in claim 4 is also directed to the properties of the dosage form. The product in Kigoshi is also spray dried and the solvent is removed by vacuum drying, spray-drying or freeze-drying and the dried product is inherently free of solvent and Kigoshi did not say that the product has associated solvent so that claim 50 is met and further because the spray dried solid dispersion of both the claims and that of the prior art are prepared by the same process of spray drying.

13. For new claim 58, because the spray dried solid dispersion of the claims and the prior art are prepared by the same process, the spray dried solid dispersion of Miyajima is inherently supersaturated in the drug.

14. The spray dried solid dispersion containing the drug and the HPMCAS meets the limitation of the amended claims where the spray dried solid dispersion consists of the drug and

polymer and specifically, Kigoshi dissolves the drug and HPMCAS in common solvent and removes the solvent by spray drying.

15. Claims 1, 4, 49, 53, 54, 55 and 56 and 58 are rejected under 35 U.S.C. 102(b) as being anticipated by HIKOSAKA JP 57-176907 (Eng. Translation provided by applicant in 1449 filed 5/07/2001).

16. JP 57-176907 discloses composition comprising AS-56C in substantially amorphous form in one or more bases selected from hydroxypropyl methyl cellulose phthalate, HPMCAS, methyl acrylate-methacrylic acid-methacrylate copolymers and methacrylic acid-methyl methacrylate copolymers (first full paragraph of page 2); the AS-56C and HPMCAS are dissolved in organic solvent and the product is obtained by spray drying (4th full paragraph page 2); the ratio of drug AS-56C to polymer ranges from 1:4, 1:3, 1:2, 1:20 in Examples 1-12. The ratios meet the ratio requirements for the drug to polymer of claims 1, 55 and 56. Claims 4, 49, 53 and 54 recite the properties of the composition so that these claims are met. Since the composition of JP 57-176907 spray dried just as the claimed composition, the composition of the JP 57-176907 is inherently a spray dried solid dispersion and is molecularly dispersed.

17. For new claim 58, because the spray dried solid dispersion of the claims and the prior art are prepared by the same process, the spray dried solid dispersion of Miyajima is inherently supersaturated in the drug.

18. The spray dried solid dispersion the drug and the HPMCAS meets the limitation of the amended claims where the spray dried solid dispersion consists of the drug and polymer.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

21.

22. Claims 1, 23, 50 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyajima et al. (EP 0 344 603) or Kigoshi et al. (EP 0 784 974).

23. Miyajima: Miyajima is described above as anticipating claim 1. For claims 50 and 51, since the formulation of Miyajima and that of the instant claims are spray dried, it would be reasonable to expect that the residual solvent in the formulation of Miyajima and the composition of the claims would be the same except where applicant shows that to not be the case. Although, Miyajima's spray dried formulations are granules, Miyajima does not specifically say that the particle size is less than 100 μm in diameter as recited in claim 23. But, the particle size of 100-400 or 150-300 mesh of the Miyajima particles encompasses the particles size of 100

micron since 400 and 300 mesh size are less than 100 micron, and anticipates less than 100 micron because, the particles of Miyajima at 400 or 300 mesh (37 μm and 53-44 μm) are less than 100 micron. Therefore, in the alternative, taking the teachings of Miyajima, one having ordinary skill in the art at the time the invention was made, would reasonably expect that the particles of the dispersion would have sizes that are less than 100 μm according to the disclosed size of 100-400 and 150-300 mesh (149-37 μm and about 105-44 μm) according to the disclosure of Miyajima.

24. Kigoshi: Kigoshi has been described above as anticipating claim 1. For claims 50 and 51, since the formulation of Kigoshi and that of the instant claims are spray dried, it would be reasonable to expect that the residual solvent in the formulation of Kigoshi and the composition of the claims would be the same except there is factual evidence that it's not. Although, Kigoshi's spray dried formulations are granules, Kigoshi does not specifically teach the particle size of claim 23. But, in example 1, the particle size is 200 mesh (74 μm) and since other polymers such as the HPMCAS are contemplated (see claims 5 and 6), it is reasonable to expect that when the other polymers such as hydroxypropylmethyl cellulose phthalate, hydroxypropylmethyl cellulose acetate succinate, or carboxymethylethyl cellulose (see claims 5 and 6) are used, the drug and polymer solution when also be sprayed onto a seed of 200 mesh (74 μm) would form dispersed solids having size of 200 mesh (74 μm) which is less that 100 micron. Therefore, taking the teachings of Kigoshi, one having ordinary skill in the art at the time the invention was made would reasonably expect that solution of drug and HPMCAS when sprayed onto a core particle having the size of 200 mesh (74 μm) would expectedly result in dispersion of drug and HPMCAS having a size of 74 μm, which is less than 100 μm.

25. Claims 1, 4, 36, 37 49-51 and 53-56 rejected under 35 U.S.C. 103(a) as being unpatentable over Kigoshi et al. (EP 0 784 974) in view of Madhusoodanan et al. ("Efficacy of risperidone treatment for psychoses associated with schizophrenia, schizoaffective disorder, bipolar disorder, or senile dementia in 11 geriatric patients: a case series," in J. Clin. Psychiatry, 1995 Nov;56(11):514-8 (Abstract enclosed)) and further in view of Bymaster et al. (US 6,147,072).

26. Kigoshi has been described as teaching the limitations of claim 1 and dependent claims 4, 49-51 and 53-56. The active agents in Kigoshi are xanthine derivatives and these derivatives have anti-dementia activity in addition to diuretic activity, kidney protecting activity and cerebral function-improving activity (page 2, lines 5-8).

27. The xanthine derivatives are not the antipsychotic drugs of claims 36 and 37. But, drugs such as the antipsychotic drug, risperidone is known in the art to have effect on psychosis related to dementia, bipolar disorder and schizophrenia according to the abstract of Madhusoodanan in J. Clin. Psychiatry, 1995 Nov. Further also, risperidone and ziprasidone are known anti-psychotic drugs (see Bymaster at column 2, lines 22 and 43). One anti-dementia agent can be used in place of the other with the expectation that either will deliver the desired anti-dementia effect.

28. Therefore, taking the teachings of Kigoshi, Madhusoodanan and Bymaster, one having ordinary skill in the art at the time the invention was made would reasonably expect that solid dispersions obtained by substituting ziprasidone for the xanthine derivatives in Kigoshi would have the expected anti-dementia activity in a person in need thereof.

29.

Response to Arguments

30. Applicant's arguments filed 5/18/2011 have been fully considered but they are not persuasive.

31. Applicant on pages 6 of 11 to 10 of 11 presents the Wands Factors analyzing why the prior art references Miyajima, Kigoshi and HIKOSAKA are not enabled.

32. Response: The recitation and discussion of the Wands factors is not a factual showing that the person of ordinary skill in the art would disregard the teaching of Miyajima, Kigoshi and HIKOSAKA that a drug and dispersing polymer such as HMPCAS are dissolved in common organic solvent and the solvent removed by spray drying --- this teaching is specifically disclosed in the references. Applicant has failed to present factual evidence that the drugs and the HPMCAS disclosed to be dissolved in common organic solvent in Miyajima, Kigoshi and HIKOSAKA cannot be dissolved in the common solvent. Therefore, although applicant has impressively discussed the Wands factors, there is no evidentiary showing that the drugs and HPMCAS as disclosed by Miyajima, Kigoshi and HIKOSAKA to be dissolved in common solvent and the solvent removed by freeze drying cannot be done. A prior art reference is not limited to the examples.

33. On page 7 of 10, applicant argues that Miyajima, Kigoshi and HIKOSAKA do not inherently disclose solid dispersions that have amorphous drug.

34. Response: The examiner disagrees. Applicant has failed to factually show that the drugs in the spray dried product consisting of the drug and HPMCAS is not amorphous.

35. Applicant stated on page 11 of 11 that a declaration under 37 CFR 1.132 would be filed shortly and that should be considered in conjunction with the amendment and evidence.

36. Response: As of 8/22/29, the application file does not have such a declaration under 37 CFR 1.132.

37. Remington Evidence Reference: Applicant argues that the Remington reference demonstrates that spray dried materials contain particles or crystals and/or amorphous solids depending on the rate and conditions of the solvent removal, which is to say that spray drying does not necessarily and/or inherently produce amorphous drug regardless of the conditions and that the prior art of record fails to indicate the any of the conditions that would produce amorphous solid.

38. Response: The examiner disagrees with applicant's reasoning that only certain conditions of solvent and conditions of spray drying would lead to the production of amorphous solid in view of the following:

a) The PTO does not have laboratories to provide factual evidence that the drug in the spray dried products of Miyajima, Kigoshi and HIKOSAKA is not amorphous.

B) Applicant has failed to factually show that the drug is not amorphous.

C) Applicant's solid amorphous dispersion is obtained by spray drying and there is no disclosure of the conditions applicant may be referring to that must be present in order for the drug to be amorphous.

D) Applicant has not provided a list of solvents and the conditions that are necessary for a drug dissolved in that solvent together with HPMCAS that when spray dried would lead to amorphous drug.

E) Applicant has not provided factual evidence that the drugs in the spray dried products of Miyajima, Kigoshi and HIKOSAKA are not amorphous.

39. No claim is allowed.

40. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

41. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

42. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on Monday to Thursday from 7 a.m. to 5:30 p.m.

43. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Y. Kwon can be reached on (571) 272-0581. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

44. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR

system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Blessing M. Fubara/
Primary Examiner, Art Unit 1613